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| <b>PETITION FOR CERTIFICATE OF CORRECTION</b><br><br>Address to:<br>Mail Stop Certificate of Correction Branch<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, VA 22313-1450 | Attorney Docket      | GHDX-008   |
|  | First Named Inventor | Cobleigh, Melody A.  |
|  | Patent Number        | 7,569,345  |
|  | Issue Date           | August 4, 2009   |
|  | Application Number   | 10/758,307   |
|  | Filing Date          | January 14, 2004   |
|  | Title:               | <i>"Gene Expression Markers for Breast Cancer Prognosis"</i> |

Sir:

Transmitted herewith for filing is a Certificate of Correction for the above-identified patent. Please correct the following:

**In the Claims:**

- Claim 3, column 181, line 22: Following "wherein" delete "said".
- Claim 14, column 182, line 34: Following "level of" insert "a".
- Claim 14, column 182, line 36: Replace "Her2negatively" with "Her2 negatively"

Attached herewith is a copy of an Amendment filed on December 2, 2008 with the correct claim numbers 8 and 59, now renumbered 1 and 14, to support our request for correction.

It is believed that no fee is due since the error was made by the Patent and Trademark Office. However, the Commissioner is hereby authorized to charge any fees under 37 C.F.R. § 1.20, which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815 order number GHDX-008.

Respectfully submitted,

BOZICEVIC, FIELD & FRANCIS LLP

Date: December 14, 2009

By: /James S. Keddie, Reg. No. 48,920/  
James S. Keddie, Ph.D.  
Registration No. 48,920

BOZICEVIC, FIELD & FRANCIS LLP  
1900 University Avenue, Suite 200  
East Palo Alto, California 94303  
Telephone: (650) 327-3400  
Fax: (650) 327-3231

## UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

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PATENT NO. : 7,569,345  
APPLICATION NO.: 10/758,307  
ISSUE DATE : August 4, 2009  
INVENTOR(S) : Cobleigh, Melody A.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

### In the Claims:

- Claim 3, column 181, line 22: Following “wherein” delete “said”.
- Claim 14, column 182, line 34: Following “level of” insert “a”.
- Claim 14, column 182, line 36: Replace “Her2negatively” with “Her2 negatively”

MAILING ADDRESS OF SENDER (Please do not use customer number below):

**BOZICEVIC, FIELD & FRANCIS LLP**  
1900 University Avenue, Suite 200  
East Palo Alto, California 94303

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| <b>AMENDMENT UNDER<br/>37 C.F.R. §1.111</b><br><br>Address to:<br>Mail Stop: Amendment<br>P.O. Box 1450<br>Alexandria, VA 22313-1450 | Attorney Docket No.  | GHDX-008  |
|  | Confirmation No.     | 5600  |
|  | First Named Inventor | Cobleigh, Melody A.                                   |
|  | Application Number   | 10/758,307  |
|  | Filing Date          | January 14, 2004                                      |
|  | Group Art Unit       | 1636  |
|  | Examiner Name        | Qian, Celine X.                                       |
|  | Title:               | "Gene Expression Markers for Breast Cancer Prognosis" |

Sir:

This amendment is responsive to the Office Action dated July 11, 2008, for which a three-month period for response was given, making this response due on October 11, 2008.

Applicants petition for a two-month extension of time, making this amendment due on December 11, 2008. Accordingly, this response is timely filed.

In view of the remarks put forth below, reconsideration and allowance are respectfully requested.

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## I. AMENDMENTS

### AMENDMENTS TO THE SPECIFICATION

Please also amend the Specification at page 28, paragraph [0098], as follows:

Twenty patients with normalized CT for estrogen receptor (ER)  $[[< 1.6]] \leq 0$  (i.e., ER negative patients) were subjected to separate analysis. A t test was performed on the two groups of patients classified as either no recurrence and no breast cancer related to death at three years, or recurrence or breast cancer-related death at three years, and the p-values for the differences between the groups for each gene were calculated. Table 3 lists the genes where the p-value for the differences between the groups was  $<.118$ . The first column of mean expression values pertains to patients who neither had a metastatic recurrence nor died from breast cancer. The second column of mean expression values pertains to patients who either had a metastatic recurrence of or died from breast cancer.--

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AMENDMENTS TO THE CLAIMS

Please amend the claims as set out in the listing below.

1. (Currently amended) A method of predicting the likelihood of long-term survival of an ~~without recurrence of breast cancer for a patient having estrogen receptor (ER)-positive breast cancer patient without the recurrence of breast cancer,~~ the method comprising:

(a) assaying an expression level of an RNA transcript or its expression product in a biological sample comprising a breast cancer cell obtained from the patient, wherein the RNA transcript is a MYBL2 transcript;

(b) determining [[the]] a normalized expression level of the MYBL2 RNA transcript of MYBL2 or its expression product, in an ER-positive breast cancer tissue sample obtained from said patient, normalized against the expression level of all RNA transcripts or their products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their expression products and wherein the normalized expression level of the MYBL2 transcript or its expression product positively correlates with an increased likelihood of breast cancer recurrence in the patient; and

(b) (c) ~~providing prognostic information to the patient containing regarding an estimate of the likelihood of long-term survival without breast cancer recurrence in said for the patient, wherein the information comprises the normalized expression level of the MYBL2 transcript or its expression product-expression of the RNA transcript of MYBL2 or its expression product is an indication of a decreased likelihood of long-term survival without breast cancer recurrence.~~

2. – 5. (Canceled)

6. (Original) The method of claim 1 wherein breast cancer is invasive breast carcinoma.

7. (Canceled)

8. (Currently amended) The method of claim 1 wherein said the biological sample RNA is isolated ~~from~~ a fixed, wax-embedded breast cancer tissue specimen of said patient.

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9. (Currently amended) The method of claim 1 wherein ~~said RNA~~ the biological sample is isolated from core biopsy tissue or fine needle ~~aspirate~~ aspirated cells.

10-24. (Canceled)

25. (Currently amended) A method of preparing a personalized genomics profile for a patient with estrogen receptor (ER)-positive breast cancer, comprising the steps of:

(a) ~~subjecting RNA extracted from an estrogen receptor (ER) positive breast tissue~~ assaying an expression level of an RNA transcript or its expression product in a biological sample comprising a breast cancer cell obtained from the patient to gene expression analysis, wherein the RNA transcript is a MYBL2 transcript;

(b) determining ~~[[the]]~~ a normalized expression level of the ~~RNA MYBL2~~ transcript of MYBL2 or its expression product, ~~wherein the expression level is normalized against a control gene or genes and optionally is compared to the amount found in a breast cancer reference tissue set wherein the normalized expression level of the MYBL2 transcript or its expression product positively correlates with an increased likelihood of breast cancer recurrence in the patient;~~ and

(c) creating a report summarizing the data obtained from the normalized expression level by ~~said gene expression analysis, and containing an estimate of likelihood of long term survival without cancer recurrence in said patient, wherein expression of the RNA transcript of MYBL2 or its expression product is considered an indication of a decreased likelihood of long term survival without breast cancer recurrence.~~

26. (Canceled)

27. (Currently amended) The method of claim ~~[[26]]~~ 25, wherein ~~said breast tissue~~ the biological sample is ~~obtained from~~ a fixed, paraffin-embedded biopsy sample.

28. (Currently amended) The method of claim ~~[[27]]~~ 25 wherein ~~said~~ the RNA transcript is fragmented.

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29. (Canceled)

30. (Currently amended) The method of claim 25 further comprising wherein said report further comprises a recommendation for a treatment modality of said patient identifying a treatment option for the patient based on the normalized expression level.

31-35. (Canceled)

36. (Currently amended) The method of claim 1 wherein the expression level of the MYLB2 transcript, or its expression product, is normalized against a [[the]] reference set of RNA transcripts or their expression products comprises the comprising RNA transcripts of two or more housekeeping genes, or their expression products.

37. (Currently Amended) The method of claim 36 wherein the two or more housekeeping genes are selected from the group consisting of glyceraldehyde-3-phosphate dehydrogenase (GAPDH), Cyp1, albumin, actins, tubulins, cyclophilin, hypoxanthine phosphoribosyltransferase (HRPT), L32, 28S, and 18S.

38. - 55. (Canceled)

56. (Withdrawn- currently amended) The method of claim 1, further comprising  
(a) assaying an expression level of at least one RNA transcript or its expression product in a biological sample comprising at least one breast cancer cell obtained from the patient, wherein the at least one RNA transcript is the transcript of a gene selected from the group consisting of: GRB7, CTSL, CD68, Chk1, AIB1, CCNB1, MCM2, FBXO5, STK15, SURV, EGFR, HIF1 $\alpha$ , and TS;

(b) determining the a normalized expression level of one or more the RNA transcripts transcript or their its expression products product in a breast cancer tissue sample obtained from said patient, normalized against the expression level of all RNA transcripts or their products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their expression products, wherein the RNA transcript is the transcript of one or more genes selected from the

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~~group consisting of: TP53BP2, Bcl2, KRT14, IRS1, GRB7, CTSL, CD18, EstR1, Chk1, IGFBP2, BAG1, CEGP1, STK15, GSTM1, FHIT, RIZ1, AIB1, SURV, BBC3, IGF1R, p27, GATA3, ZNF217, EGFR, CD9, HIF1 $\alpha$ , pS2, ErbB3, TOP2B, MDM2, RAD51C, KRT19, TS, KLK10,  $\beta$ -Catenin,  $\gamma$ -Catenin, MCM2, PI3KC2A, IGF1, TBP, CCNB1, FBXO5, and DR5,~~  
wherein the normalized expression level of the RNA transcript or its expression product positively correlates with an increased likelihood of breast cancer recurrence; and

(c) providing information comprising the likelihood of long-term survival without breast cancer recurrence for the patient, wherein the information comprises the normalized expression level of the RNA transcript or its expression product.

57. (Withdrawn- currently amended) The method of claim [[56]] 1, further comprising

(a) assaying an expression level of at least one RNA transcript or its expression product in a biological sample comprising at least one breast cancer cell obtained from the patient, wherein the at least one RNA transcript is the transcript of a gene selected from the group consisting of: TP53BP2, Bcl2, KRT14, EstR1, IGFBP2, BAG1, CEGP1, KLK10,  $\beta$ -Catenin,  $\gamma$ -Catenin, DR5, PI3KCA2, RAD51C, GSTM1, FHIT, RIZ1, BBC3, TBP, p27, IRS1, IGF1R, GATA3, ZNF217, CD9, pS2, ErbB3, TOP2B, MDM2, IGF1, and KRT19;

(b) determining a normalized expression level of the at least one RNA transcript or its expression product, wherein expression of one or more of GRB7, CTSL, CD68, Chk1, AIB1, CCNB1, MCM2, FBXO5, STK15, SURV, EGFR, HIF1 $\alpha$ , and TS indicates a decreased likelihood of long term survival without breast cancer recurrence, and the expression of one or more of TP53BP2, Bcl2, KRT14, EstR1, IGFBP2, BAG1, CEGP1, KLK10,  $\beta$ -Catenin,  $\gamma$ -Catenin, DR5, PI3KCA2, RAD51C, GSTM1, FHIT, RIZ1, BBC3, TBP, p27, IRS1, IGF1R, GATA3, ZNF217, CD9, pS2, ErbB3, TOP2B, MDM2, IGF1, and KRT19 indicates an increased likelihood of long term survival without breast cancer recurrence  
the normalized expression level of the at least one RNA transcript or its expression product negatively correlates with a an increased likelihood of breast cancer recurrence.

58. (Withdrawn - currently amended) The method of claim 1 further comprising determining the normalized expression level of prognostic RNA transcripts a PR RNA transcript or their its expression products product of PR, wherein the ~~expression of PR indicates an~~



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increased likelihood of long-term survival without breast cancer recurrence the normalized expression level of PR negatively correlates with an increased likelihood of breast cancer recurrence.

59. (Withdrawn - currently amended) The method of claim [[58]] 1 further comprising determining [[the]] a normalized expression level of prognostic RNA transcripts a Her2 RNA transcript or their its expression products product of Her2, wherein the normalized expression level of Her2, indicates a decreased likelihood of long-term survival without breast cancer recurrence negatively correlates with an increased likelihood of long-term survival without breast cancer recurrence .

60. (Withdrawn – currently amended) The method of claim 1 further comprising in step (a) determining the expression level of the PR RNA transcript ~~of PR~~ or its expression product in a breast cancer tissue sample obtained from said patient, normalized against the expression levels of all RNA transcripts or their expression products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their products.

61. (Withdrawn – currently amended) The method of claim 1 or claim 60 further comprising in step (a) determining the expression level of the Her2 RNA transcript ~~of Her2~~ or its expression product in a breast cancer tissue sample obtained from said patient, normalized against the expression levels of all RNA transcripts or their expression products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their products.

62. (Withdrawn) The method of claim 25 further comprising in step (b) determining the expression level of PR, wherein the expression level is normalized against a control gene or genes and optionally is compared to the amount found in a breast cancer reference tissue set.

63. (Withdrawn) The method of claim 25 or claim 62 further comprising in step (b) determining the expression level of Her2 wherein the expression level is normalized against a control gene or genes and optionally is compared to the amount found in a breast cancer reference tissue set.

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64.- 66. (Canceled)

67. (New) The method of claim 1, wherein the information is provided in the form of a report.

68. (New) The method of claim 56, wherein the information is provided in the form of a report.

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## II. REMARKS

### FORMAL MATTERS

Claims 1, 6, 8-9, 25-28, 30, 36-37, 53, and 56-66 were pending prior to entry of the above amendment.

Claims 26, 53, and 64-66 are hereby canceled without prejudice or disclaimer.

Claims 67-68 are newly added.

Claims 1, 8, 9, 25, 27-28, 30, 36, 37, 56-61 are hereby amended to clarify aspects of the claimed invention and resolve antecedent basis issues.

Support for the amended and newly added claims can be found in at least paragraphs [0003], [0040], [0044], [0079], and [0090]-[0097], and Tables 1, 2 and 4 of the specification, and the original claims as filed.

Accordingly, claims 1, 6, 8-9, 25, 27-28, 30, 36-37, 56-63, and 67-68 are now pending, with claims 56-63 pending, but withdrawn from consideration. It is noted that new claim 68 may be deemed withdrawn in view of its dependency upon claim 56, which is presently withdrawn.

Claims 56-63 and Claims 1 and 25 are independent. The remaining claims depend, directly or indirectly, from independent claims 1 and 25.

No new matter is added.

### INTERVIEW SUMMARY

Applicants wish to express their gratitude to Examiners Woitach and Qian (by telephone) for the in-person interview with Craig Wilde, Kathleen Determann, and the undersigned on October 7, 2008. The rejections of the present action were discussed during the interview, and claim amendments substantially as set out herein were discussed. Applicants have reviewed the Interview Summary dated October 16, 2008, and agree with the Examiner as to the substance of the interview.

### RESTRICTION REQUIREMENT

Applicants thank the Examiner for acknowledging that claims 56-63 will be rejoined upon allowance of claims 1 and 25. Applicants request that the Examiner acknowledge that new

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claim 68, which depends directly from withdrawn claim 56 and indirectly from claim 1, will also be rejoined upon allowance of claim 1.

Claims 65 and 66 have been withdrawn from consideration as being directed to a non-elected invention. However, as these claims have been canceled, this restriction requirement is moot and Applicants respectfully ask that it be withdrawn.

## **REJECTIONS UNDER 35 USC § 112**

Claims 1, 6, 8, 9, 25-28, 30, 36, 37, 53, and 64 stand rejected under 35 USC § 112, first paragraph, as “failing to comply with the enablement requirement.” (*See*, OA at p. 3.) Claims 26, 53, and 64 have been canceled, therefore the rejection to these claims is moot and Applicants respectfully request that it be withdrawn. To the extent that this rejection also applies to amended claims 1, 6, 8, 9, 25, 27-28, 30, and 36-37, Applicants respectfully traverse it.

To be enabled, the specification must describe the invention in such terms that one skilled in the art can make and use the invention. MPEP § 2164. Not everything necessary to practice the invention need be disclosed. All that is necessary is that one skilled in the art be able to practice the claimed invention, given the knowledge and skill in the art. Further, the scope of enablement must only bear a “reasonable correlation” to the scope of the claims. MPEP § 2164.08. Thus, the enablement requirement is met if the specification enables one mode of making the invention. *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1361 (Fed. Cir. 1998). An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance. MPEP § 2164.06.

## **Breadth of claim, teaching of specification, degree of experimentation**

### ***Mere presence of mRNA***

The Examiner has interpreted the claims as encompassing a method for predicting breast cancer recurrence “by the mere presence of MYBL2 expression of both mRNA and protein.” (*See*, OA at p. 4, 7.) However, amended claims 1 and 25, upon which the other claims depend, directly or indirectly, describe a method comprising assaying an expression level of an RNA transcript of MYBL2, or its expression product, and normalizing that expression level, wherein the normalized expression level of the MYBL2 transcript, or its expression product, positively

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correlates with the likelihood of breast cancer recurrence in the patient. The Examiner has conceded that the specification establishes "a correlation between breast cancer recurrence or death and the higher expression of the mRNA transcripts of the sequence disclosed in NM\_002466." (See, OA at p. 4-5, 7.) Applicants agree that such a correlation *is* established in the specification as filed.

The specification provides data from an example in which a t test assuming equality of variance was performed on the groups of patients classified as either having no recurrence and no breast cancer related death at three years, versus recurrence, or breast cancer-related death at three years, and the p-values for the difference in mean expression between the groups. (See, Specification at paragraphs [0090]-[0099].) Table 1 lists 47 genes for which the p-value for differences between the groups in mean expression was less than 0.10. The first column of mean expression values pertains to patients who neither had a metastatic recurrence of, nor died from, breast cancer. The second column of mean expression values pertains to patients who either had a metastatic recurrence of, or died from, breast cancer.

Similarly, Tables 2 and 3 present results for the subsets of ER positive and negative patients. In Table 2 there are 57 patients with normalized CT for estrogen receptor ER > 0 (i.e. ER positive patients). A t test was performed on the two groups of patients classified as either no recurrence or no breast cancer related death at three years, or recurrence or breast cancer related death at three years, and p-values for the differences between the groups for each gene were calculated. The first column of mean expression values pertains to patients who neither had a metastatic recurrence nor died from breast cancer. The second column of mean expression values pertains to patients who either had a metastatic recurrence of or died from breast cancer. Table 2 lists genes where the p-value for the differences between groups was less than 0.1. (See, also, Specification at paragraphs [0095]-[0098].) The resulting t-tests provide evidence of a statistically significant difference in mean normalized expression measurement between patients with breast cancer recurrence and patients without breast cancer recurrence. These results are indicative of a significant association of gene expression with likelihood of breast cancer recurrence.

The ordinarily skilled artisan would recognize that the data in the tables in the specification may be used to construct a curve showing a positive correlation of MYBL2 normalized gene expression values and increasing likelihood of breast cancer recurrence. For

example, the ordinarily skilled artisan can apply logistic regression analysis to model the probability of breast cancer recurrence as a function of gene expression measurement ( $C_T$ ). For example, Appendix A provides results from logistic regression analysis for recurrence or breast cancer related death at three years, respectively, for the corresponding genes provided in Table 2. Results reveal that, as expected, the resulting p-values from the likelihood ratio tests of significance of gene expression measurement under the logistic model are very close to the p-values generated by the corresponding t-tests. (*See, e.g.*, Specification at paragraphs [0100]-[0107].)

Appendix B provides a predicted probability plot of recurrence or breast cancer related death at 3 years, for ER positive patients, as a function of MYBL2 expression along with 95% confidence intervals. The "Estimate" number for MYBL2 from Appendix A represents the slope of the curve in Appendix B, and "AUC" (App. A) the curve inflection point. Logistic regression analysis may be used to relate data, including the "Odds Ratio" and "Estimate" from Appendix A, to determine predictive probability of response. Thus, the specification illustrates that the greater the normalized MYBL2 expression values, the worse the prognosis for breast cancer patients.

Thus, the specification provides sufficient details to allow one skilled in the art to predict the likelihood breast cancer recurrence or death based on expression levels of MBYL2.

#### ***Correlation at the protein level***

The Examiner has taken the position that "the specification does not teach whether this correlation is also observed at protein level." (*See*, OA at p. 5, 7.) As a general rule, however, a correlation between RNA levels and protein expression is known in the art. *See, e.g., Amgen v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1298 (Fed. Cir. 2006). Members of the MYB family proteins have been found to perfectly correlate with corresponding mRNA levels. (*See, e.g.,* Lacoste, et al., British Journal of Haematology, 138:487-501 (2007) (MYB expression in lymphoma cells) (Exhibit A). Absent evidence to the contrary, the ordinary artisan would reasonably expect that mRNA levels in cancer would correlate to the levels of associated protein(s). *Ex part Lee*, 2008 WL 447537 (BPAI 2008): ("As the Examiner has not provided any evidence to dispute the reasonably calculated correlation between...mRNA levels and [associated] protein levels, the rejection cannot be sustained.")

*Orthologs and splice variants*

The Examiner also indicates that MYBL2 refers to myeloblastosis oncogene-like 2 as well as “orthologs wherein the sequences are substantially different from each other ... and splice variants which may exist, but their full-length nature have not been determined.” (See, OA at p. 4.) However, the enablement requirement allows for a reasonable amount of experimentation to determine if an invention is applicable to splice variants. *US v. Telectronics*, 857 F.2d 778 (Fed. Cir. 1988).

The MYBL2 gene is identified in the specification using the Genbank accession no., NM\_002466, defined therein as Homo sapiens v-myb myeloblastosis viral oncogene homolog (avian)-like 2. According to the annotated summary by the NCBI staff, “[t]ranscript variants may exist for this gene, but their full-length natures have not been determined.” (Emphasis added.) Thus, there is currently no definitive evidence that splice variants existed at the time the application was filed. The Examiner has provided no evidence to the contrary.

Nonetheless, even if the existence of MYBL2 splice variants *were* confirmed in the future, the specification would still be sufficient to allow one skilled in the art to determine which sequences would be associated with likelihood of breast cancer recurrence. For example, using the amplicon sequence provided in Table 5A of the specification, one could simply conduct a BLAST search to determine which of the isoforms would have been measured using the disclosed invention. Therefore, it would require only a reasonable amount of experimentation to confirm which MYBL2 sequences were amplified in the examples provided in the specification, and to design probe/primers to amplify a conserved region.

*State of the art*

The Examiner takes the position that “the prior art teaches that there are many factors that need to be considered in order to develop a reliable genetic test.” (See, OA at p. 7.) However, Applicants respectfully assert that the references cited (OA, p. 5-7) do not establish a reasonable basis to question the enablement provided for the claimed invention. MPEP § 2164.05. First, references to literature concerning the predictability of disease diagnostics<sup>1</sup> are inapposite as the

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<sup>1</sup> The post-filing references, Kroese, et al., *Genetics in Medicine*, Vol. 6:475-480 (2004), and Lucentini, et al., *The Scientist*, p. 20 (Dec. 20, 2004) both concern studies correlating gene expression with disease states. (See, OA at p. 10.)

claimed method involves patients who have independently been diagnosed with breast cancer.

(*See, e.g.*, Specification, paragraphs [0010] and [0082].)

Second, the references concerning gene profiling actually teach that validated assays supported by statistically meaningful data are reliable. For example, Shalon et al. (US 2001/0051344 A1, Dec. 13, 2001) (hereinafter "Shalon") indicate that when differences in expression "persist in comparison of the averaged gene expression patterns from [two populations], it becomes more likely that the expression of that particular gene is related to the shared phenotype of the test individuals...Standard statistical analyses may be applied to determine when the messenger nucleic acids from a sufficient number of individuals [at least 5] have been evaluated for differences in gene expression." (Shalon at paragraphs [0155]-[0156].) Similarly, other references cited by the Examiner support the powerful potential of gene expression profiling that, like the instant invention, is clinically validated<sup>2</sup> and incorporates reproducible quality control.<sup>3</sup>

Finally, the application as filed provides evidence of the association of normalized MYBL2 gene expression levels and breast cancer recurrence. As noted above, the specification includes data in Tables 1, 2, and 3 that provides evidence of a statistically significant difference in mean normalized expression measurement between patients with breast cancer recurrence and patients without breast cancer recurrence for MYBL2. These results are indicative of a significant association of normalized expression of MYBL2 with increased likelihood of breast cancer recurrence.

In view of the above, Applicants respectfully assert that the Examiner has failed to present evidence that the specification, at the time filed, would not have taught one skilled in the art how to make and/or use the full scope of the amended claims without undue experimentation. MPEP § 2164.01(a). Therefore, Applicants respectfully request that the rejection be withdrawn.

### **Claim 30**

The Examiner indicates that "the specification does not teach what sort of treatment is recommended based on the expression of MYBL2." (*See*, OA at p.4, 7.) Amended claim 30 describes identifying a treatment option for the patient based on the normalized expression level of MYBL2. Where different arts are involved in the invention, the specification is enabling if it

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<sup>2</sup> Murphy, et al., Pathology, 37(4):271-277 (2005).



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enables persons skilled in each art to carry out the aspect of the invention applicable to their specialty. MPEP § 2164.05(b). In this case, the information provided by the claimed method would help inform a treatment recommendation by a medical professional based on the current standard of care. (*See*, Specification at paragraph [0003].) For example, in breast cancer, treatment recommendations are available from the National Comprehensive Cancer Network and the American Society of Clinical Oncology.

For these reasons, Applicants respectfully assert that amended claim 30 is supported by the specification, and request that this rejection be withdrawn.

**Claim 53**

The Examiner indicates that “the specification does not teach how the reference control cancer sample is chosen.” (*See*, OA at p. 7.) As claim 53 has been canceled, this rejection is moot. Applicants respectfully request that the rejection be withdrawn.

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<sup>3</sup> Koree, et al., Current Pharmacogenomics, Vol. 3:201-216 (2005).

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### III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number GHDX-008.

Respectfully submitted,  
BOZICEVIC, FIELD & FRANCIS LLP

Date: December 2, 2008

By: /Carol L. Francis, Reg.No.36513/  
Carol L. Francis, Ph.D.  
Registration No. 36,513

Enclosures:

Appendices A and B

Exhibit 1: Lacoste, et al., British Journal of Haematology, 138:487-501 (2007)

BOZICEVIC, FIELD & FRANCIS LLP  
1900 University Avenue, Suite 200  
East Palo Alto, California 94303  
Telephone: (650) 327-3400  
Facsimile: (650) 327-3231

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